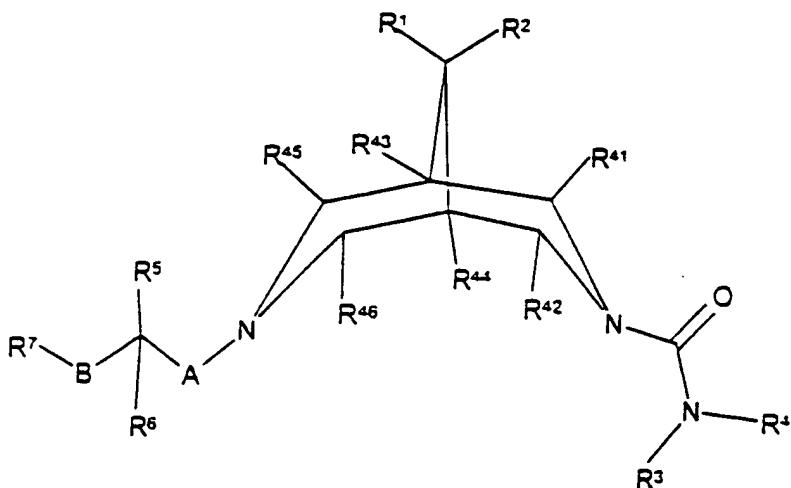


IN THE CLAIMS

Please substitute the following amended claims for corresponding claims previously presented. A copy of the amended claims showing current revisions is attached.

1 (currently amended). A compound of formula I,



wherein

R¹ and R² independently represent H, C₁₋₄ alkyl, OR^{2b} or N(R^{2c})R^{2d}, or together form -O-(CH₂)₂-O-, -(CH₂)₃-, -(CH₂)₄- or -(CH₂)₅-;

R^{2b}, R^{2c} and R^{2d} independently represent H or C₁₋₆ alkyl;

R³ represents H, C₁₋₆ alkyl or, together with R⁴, represents C₃₋₆ alkylene (which alkylene group is optionally interrupted by an O atom and/or is optionally substituted by one or more C₁₋₃ alkyl groups);

R^4 represents H, C_{1-12} alkyl, C_{1-6} alkoxy (which latter two groups are both optionally substituted and/or terminated by one or more substituents selected from -OH, halo, cyano, nitro, C_{1-4} alkyl and/or C_{1-4} alkoxy), $-(CH_2)_q$ -aryl, $-(CH_2)_q$ -oxyaryl, $-(CH_2)_q$ -Het¹ (which latter three groups are optionally substituted (at the $-(CH_2)_q$ - part and/or the aryl/Het¹ part) by one or more substituents selected from -OH, halo, cyano, nitro, $-C(O)R^{10}$, $-C(O)OR^{11}$, $-N(H)S(O)_2R^{11a}$, C_{1-6} alkyl and/or C_{1-6} alkoxy), $-(CH_2)_qN(H)C(O)R^8$, $-(CH_2)_qS(O)_2R^8$, $-(CH_2)_qC(O)R^8$, $-(CH_2)_qC(O)OR^8$, $-(CH_2)_qC(O)N(R^9)R^8$ or, together with R^3 , represents C_{3-6} alkylene (which alkylene group is optionally interrupted by an O atom and/or is optionally substituted by one or more C_{1-3} alkyl groups);

q represents 0, 1, 2, 3, 4, 5 or 6;

R^8 represents H, C_{1-6} alkyl, aryl (which latter group is optionally substituted and/or terminated by one or more substituents selected from -OH, halo, cyano, nitro, $-C(O)R^{10}$, $-C(O)OR^{11}$, $-N(H)S(O)_2R^{11a}$, C_{1-6} alkyl and/or C_{1-6} alkoxy) or, together with R^9 , represents C_{3-7} alkylene;

R^9 represents H, C_{1-4} alkyl or, together with R^8 , represents C_{3-7} alkylene;

Het¹ represents a five to twelve-membered heterocyclic ring containing one or more heteroatoms selected from oxygen, nitrogen and/or sulfur, and which also optionally includes one or more =O substituents;

R^{41} , R^{42} , R^{43} , R^{44} , R^{45} or R^{46} independently represent H or C_{1-3} alkyl;

R^5 represents H, halo, C_{1-3} alkyl, $-OR^{12}$, $-N(R^{13})R^{12}$ or, together with R^6 , represents $=O$;

R^6 represents H, C_{1-4} alkyl or, together with R^5 , represents $=O$;

R^{12} represents H, C_{1-6} alkyl, $-S(O)_2C_{1-4}$ -alkyl, $-C(O)R^{14}$, $-C(O)OR^{14}$, $-C(O)N(R^{15})R^{15a}$ or aryl (which latter group is optionally substituted and/or terminated by one or more substituents selected from -OH, halo, cyano, nitro, $-C(O)R^{10}$, $-C(O)OR^{11}$, $-N(H)S(O)_2R^{11a}$, C_{1-6} alkyl and/or C_{1-6} alkoxy);

R^{13} represents H or C_{1-4} alkyl;

R^{14} represents H or C_{1-6} alkyl;

R^{15} and R^{15a} independently represent H or C_{1-4} alkyl, or together represent C_{3-6} alkylene, optionally interrupted by an O atom;

A represents a single bond, C_{1-6} alkylene, $-N(R^{16})(CH_2)_r-$ or $-O(CH_2)_r-$ (in which two latter groups, the $-(CH_2)_r-$ group is attached to the bispidine nitrogen atom);

B represents a single bond, C_{1-4} alkylene, $-(CH_2)_nN(R^{17})-$, $-(CH_2)_nS(O)_p-$, $-(CH_2)_nO-$ (in which three latter groups, the $-(CH_2)_n-$ group is attached to the carbon atom bearing R^5 and R^6), $-C(O)N(R^{17})-$ (in which latter group, the $-C(O)-$ group is attached to the carbon atom bearing R^5 and R^6), $-N(R^{17})C(O)O(CH_2)_n-$, $-N(R^{17})(CH_2)_n-$ (in which two latter groups, the $N(R^{17})$ group is attached to the carbon atom bearing R^5 and R^6) or $-(CH_2)_mC(H)(OH)(CH_2)_n-$ (in which latter group, the $-(CH_2)_m-$ group is attached to the carbon atom bearing R^5 and R^6);

m represents 1, 2 or 3;

n and r independently represent 0, 1, 2, 3 or 4;

p represents 0, 1 or 2;

R¹⁶ and R¹⁷ independently represent H or C₁₋₄ alkyl;

R⁷ represents C₁₋₆ alkyl, aryl or Het², all of which groups are optionally substituted and/or terminated (as appropriate) by one or more substituents selected from -OH, cyano, halo, amino, nitro, Het³, -C(O)R¹⁰, C(O)OR¹¹, C₁₋₆ alkyl, C₁₋₆ alkoxy, -N(H)S(O)₂R¹⁸, -S(O)₂R¹⁹, -OS(O)₂R²⁰, -N(H)C(O)N(H)R²¹, -C(O)N(H)R²² and/or aryl (which latter group is optionally substituted by one or more cyano groups);

Het² and Het³ independently represent a five to twelve-membered heterocyclic group containing one or more heteroatoms selected from oxygen, nitrogen and/or sulfur, and which also optionally includes one or more =O substituents;

R¹⁸, R¹⁹ and R²⁰ independently represent C₁₋₆ alkyl;

R²¹ and R²² independently represent H or C₁₋₆ alkyl (optionally terminated by cyano); and

R¹⁰ and R¹¹ independently represent, at each individual occurrence, H or C₁₋₆ alkyl;

R^{11a} represents, at each individual occurrence, C₁₋₆ alkyl;

or a salt or solvate thereof;

provided that:

(a) when A and B are both single bonds and R⁷ is aryl optionally substituted aryl with a group selected from C₁-C₄ alkyl, halogen or C₁-C₄ alkoxy, then R⁵ and R⁶ do not both represent H B-CR₅CR₆-A does not represent a C₂-C₄ alkylene group;

(b) when A represents a single bond, then R⁵ and R⁶ do not together represent =O; and

(c) when R⁵ represents -OR¹² or -N(R¹³)R¹², then:-

(i) A does not represent -N(R¹⁶)(CH₂)_r- or -O(CH₂)_r-; and/or

(ii) n does not represent 0 when B represents -(CH₂)_nN(R¹⁷)-, -(CH₂)_nS(O)_p- or -(CH₂)_nO-.

2 (original). A compound as claimed in Claim 1, wherein R' represents H.

3 (previously presented). A compound as claimed in Claim 1, wherein R² represents H.

4 (previously presented). A compound as claimed in claim 1, wherein R³ represents H; C₁₋₂ alkyl; or, together with R⁴ represents C₄₋₅ alkylene, optionally interrupted by an O atom and/or optionally substituted by one or more methyl groups.

5 (original). A compound as claimed in Claim 4, wherein R³ represents H.

6 (previously presented). A compound as claimed in claim 1, wherein R⁴ represents H; linear or branched and/or saturated or unsaturated and/or cyclic, acyclic and/or part cyclic/acyclic C₁₋₈ alkyl (which alkyl group is optionally substituted by one or more cyano or halo groups and/or is interrupted by an O atom); C₁₋₆ alkoxy; -(CH₂)_qS(O)₂R⁸, -(CH₂)_qC(O)OR⁸, -(CH₂)_qN(H)C(O)R⁸, -(CH₂)_qC(O)R⁸, (in which latter four groups, q represents 0, 1 or 2 and R⁸ represents linear or branched and/or acyclic, cyclic and/or part cyclic/acyclic C₁₋₄ alkyl, or phenyl (which phenyl group is optionally substituted by one or more cyano and/or C₁₋₃ alkyl groups)); -(CH₂)_qC(O)N(R⁹)R⁸ (in which latter group, q represents 0, 1 or 2 and R⁸ and R⁹ independently represent H, linear or branched and/or acyclic, cyclic and/or part cyclic/acyclic C₁₋₄ alkyl, or together represent C₄₋₆ alkylene); -(CH₂)_q-phenyl, -(CH₂)_q-oxyphenyl or -(CH₂)_q-Het¹ (in which latter three groups, q represents 0, 1, 2 or 3, the -(CH₂)_q- part is optionally substituted by a cyano group, and the phenyl, or Het¹, part is optionally substituted with one or more substituents selected from cyano, nitro, linear or branched C₁₋₄ alkyl, linear or branched C₁₋₄ alkoxy and N(H)S(O)₂R^{11a}); or, together with R³, represents C₄₋₅ alkylene, optionally interrupted by an O atom and/or optionally substituted by one or more methyl groups.

7 (previously presented). A compound as claimed in claim 1, wherein R⁵ represents H; fluoro; OR¹² (in which R¹² represents H, phenyl (optionally substituted by one or more methoxy groups) or C(O)N(H)R^{15a} (in which R^{15a} represents linear or branched C₁₋₄ alkyl)); -N(R¹³)(R¹²) (in which R¹² represents H, C₁₋₂ alkyl, -S(O)₂-C₁₋₂ alkyl, -C(O)R¹⁴ (in which R¹⁴ represents C₁₋₂ alkyl), -C(O)OR¹⁴ (in which R¹⁴ represents linear or branched C₁₋₅ alkyl) or -C(O)N(R¹⁵)(R^{15a}) (in which R¹⁵ independently represent H or linear or branched C₁₋₃ alkyl or together represent C₄₋₅ alkylene, which alkylene group is optionally interrupted by an O atom) and R¹³ represents H or C₁₋₂ alkyl); or, together with R⁶, represents =O.

8 (original). A compound as claimed in Claim 7, wherein R⁵ represents H, OH or -N(H)C(O)N(R¹⁵)(R^{15a}).

9 (previously presented). A compound as claimed in claim 1, wherein R⁶ represents H or C₁₋₂ alkyl or together with R⁵ represents =O.

10 (original). A compound as claimed in Claim 9, wherein R⁶ represents H.

11 (previously presented). A compound as claimed in claim 1, wherein A represents a single bond, linear or branched C₁₋₄ alkylene (which group is also optionally interrupted by O), -N(H)(CH₂)_r- or -O(CH₂)_r- (in which latter two cases r is 1 or 2).

12 (original). A compound as claimed in Claim 11, wherein A represents $-\text{CH}_2-$ or $-(\text{CH}_2)_2-$.

13 (previously presented). A compound as claimed in claim 1, wherein B represents a single bond, C_{1-4} alkylene, $-(\text{CH}_2)_n\text{O}-$, $-(\text{CH}_2)_n\text{S(O)}_2-$, $-(\text{CH}_2)_n\text{N(H)}-$ or $-\text{N(H)}(\text{CH}_2)_n-$ (in which latter four cases n is 0, 1, 2 or 3).

14 (original). A compound as claimed in Claim 13, wherein B represents a single bond, $-\text{CH}_2\text{N(H)}-$ or $-\text{CH}_2\text{O}-$.

15 (previously presented). A compound as claimed in claim 1, wherein R^7 represents linear or branched and/or acyclic, cyclic and/or part cyclic/acyclic C_{1-6} alkyl (optionally substituted and/or terminated by OH); Het^2 (optionally substituted by one or more substituents selected from cyano, C_{1-3} alkyl, phenyl (which latter group is optionally substituted with one or more cyano groups), $=\text{O}$, C(O)R^{10} (in which R^{10} is linear or branched C_{1-3} alkyl) or $\text{S(O)}_2\text{R}^{19}$ (in which R^{19} is C_{1-2} alkyl); or phenyl (optionally substituted by one or more substituents selected from cyano, nitro, linear or branched C_{1-3} alkyl, linear or branched C_{1-3} alkoxy, fluoro, chloro, C(O)N(H)R^{22} (in which R^{22} represents linear or branched and/or acyclic, cyclic and/or part cyclic/acyclic C_{1-4} alkyl, which alkyl group is optionally terminated by cyano), $\text{N(H)S(O)}_2\text{R}^{18}$ (in which R^{18} represents C_{1-2} alkyl) or Het^3).

16 (original). A compound as claimed in Claim 15, wherein R⁷ represents phenyl (substituted by a cyano group (preferably in the 4-position relative to B) and by one or more optional C(O)N(H)R²² substituent).

17 (previously presented). A compound as claimed in Claim 1, wherein R⁴¹, R⁴², R⁴³, R⁴⁴, R⁴⁵ and R⁴⁶ all represent H.

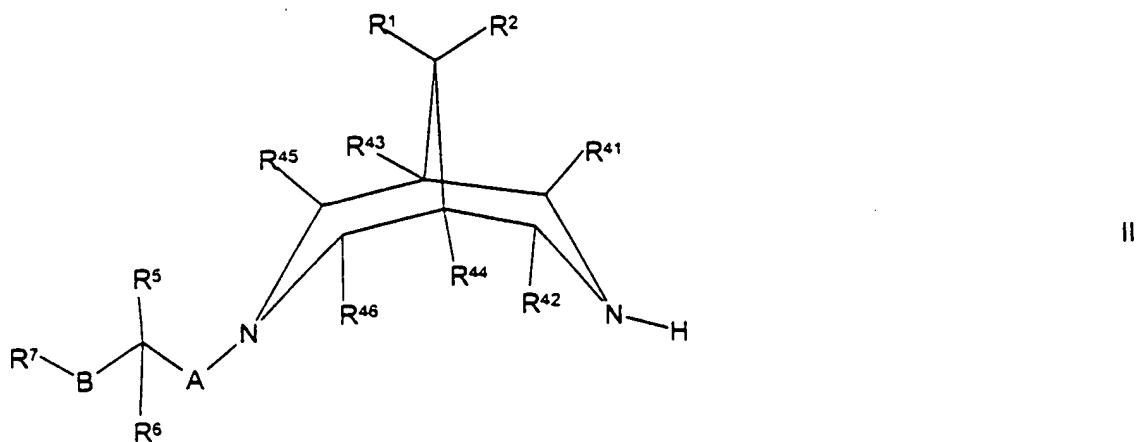
18 (previously presented). A pharmaceutical formulation including a compound as defined in Claim 1 in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier.

19-23 (cancelled).

24 (previously presented). A method of prophylaxis or treatment of an arrhythmia which method comprises administration of a therapeutically effective amount of a compound as defined in Claim 1 to a person suffering from, a susceptible to, such a condition.

25 (previously presented). A process for the preparation of a compound of formula I as defined in Claim 1 which comprises:

(a) for compounds of formula I in which R³ is H, reaction of a compound of formula II,



wherein R^1 , R^2 , R^5 , R^6 , R^7 , R^{41} , R^{42} , R^{43} , R^{44} , R^{45} , R^{46} , A and B are as defined in Claim 1 with a compound of formula III,



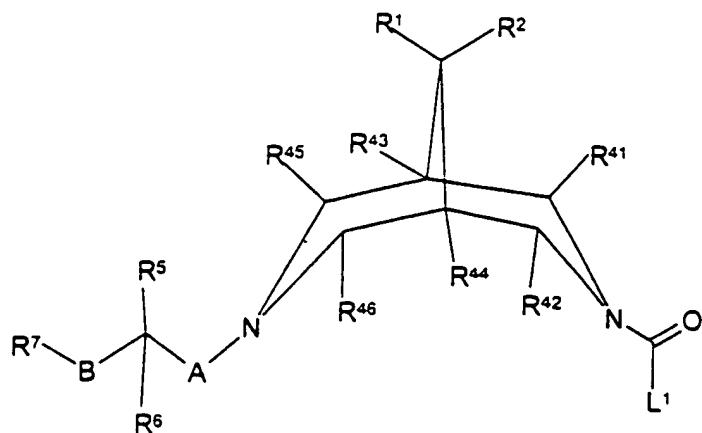
wherein R^4 is as defined in Claim 1;

(b) reaction of a compound of formula II, as defined above, with a carbonic acid derivative of formula IV,



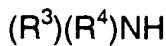
wherein L^1 represents a leaving group and R^3 and R^4 are as defined in Claim 1;

(c) reaction of a compound of formula V,



V

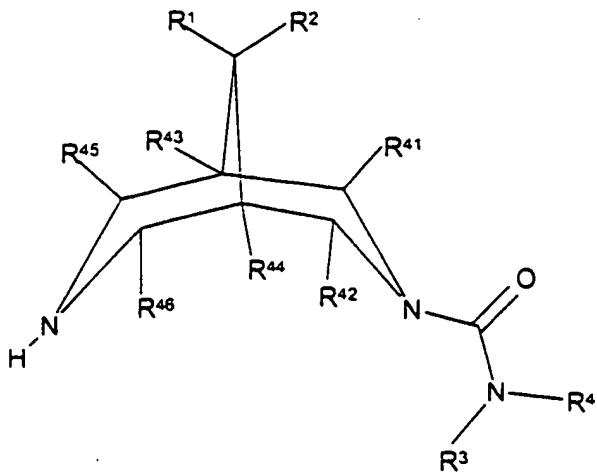
wherein and L¹ is as defined above and R¹, R², R⁵, R⁶, R⁷, R⁴¹, R⁴², R⁴³, R⁴⁴, R⁴⁵, R⁴⁶, A and B are as defined in Claim 1, with a compound of formula VA,



VA

wherein R³ and R⁴ are as defined in Claim 1;

(d) for compounds of formula I in which A represents CH₂ and R⁵ represents -OH or -N(H)R¹², reaction of a compound of formula VI,



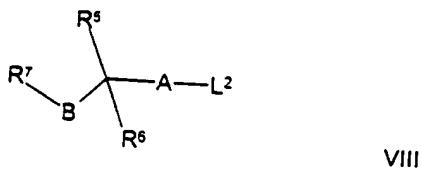
VI

wherein R^1 , R^2 , R^3 , R^4 , R^{41} , R^{42} , R^{43} , R^{44} , R^{45} and R^{46} are as defined in Claim 1,
with a compound of formula VII,



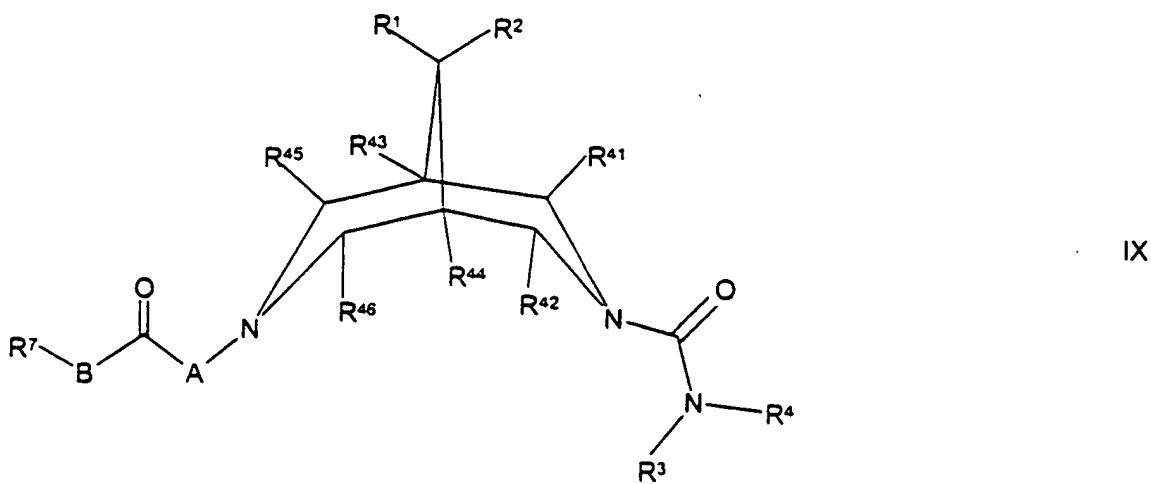
wherein X represents O or $N(R^{12})$ and R^6 , R^7 , R^{12} and B are as defined in Claim 1;

(e) reaction of a compound of formula VI, as defined above, with a compound of formula VIII,



wherein L^2 represents a leaving group and R^5 , R^6 , R^7 , A and B are as defined in Claim 1;

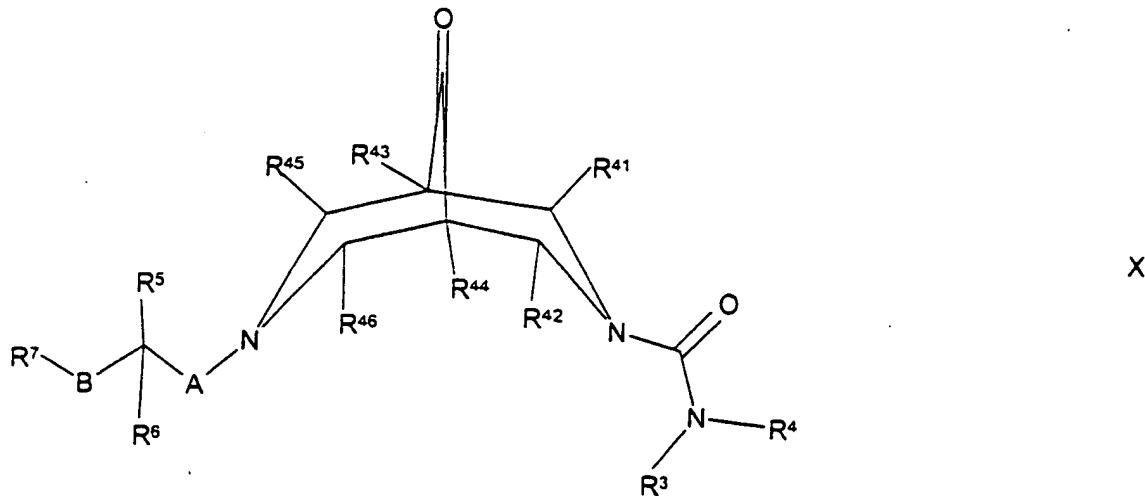
(f) for compounds of formula I in which R^5 represents H or OH and R^6 represents H , reduction of a compound of formula IX,



wherein R^1 , R^2 , R^3 , R^4 , R^7 , R^{41} , R^{42} , R^{43} , R^{44} , R^{45} , R^{46} , A and B are as defined in

Claim 1;

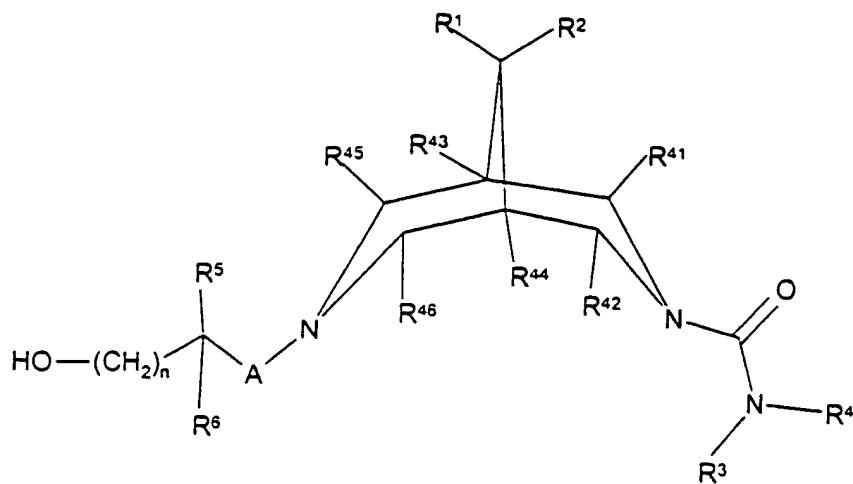
(g) for compounds of formula I in which one of R^1 and R^2 represents H or OH and the other represents H, reduction of a corresponding compound of formula X,



wherein R^3 , R^4 , R^5 , R^6 , R^7 , R^{41} , R^{42} , R^{43} , R^{44} , R^{45} , R^{46} , A and B are as defined in Claim 1;

(h) for compounds of formula I in which R^1 and R^2 together represent $-\text{O}(\text{CH}_2)_2\text{O}-$, reaction of a corresponding compound of formula X as defined above with ethane-1,2-diol;

(i) for compounds of formula I in which B represents $-(\text{CH}_2)_n\text{O}-$, reaction of a compound of formula XI,



XI

wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁴¹, R⁴², R⁴³, R⁴⁴, R⁴⁵, R⁴⁶, A and n are as defined

in Claim 1, with a compound of formula XIA,

R⁷OH

XIA

in which R⁷ is as defined in Claim 1;

(j) for compounds of formula I which are bispidine-nitrogen N-oxide

derivatives, oxidation of the corresponding bispidine nitrogen of a corresponding

compound of formula I;

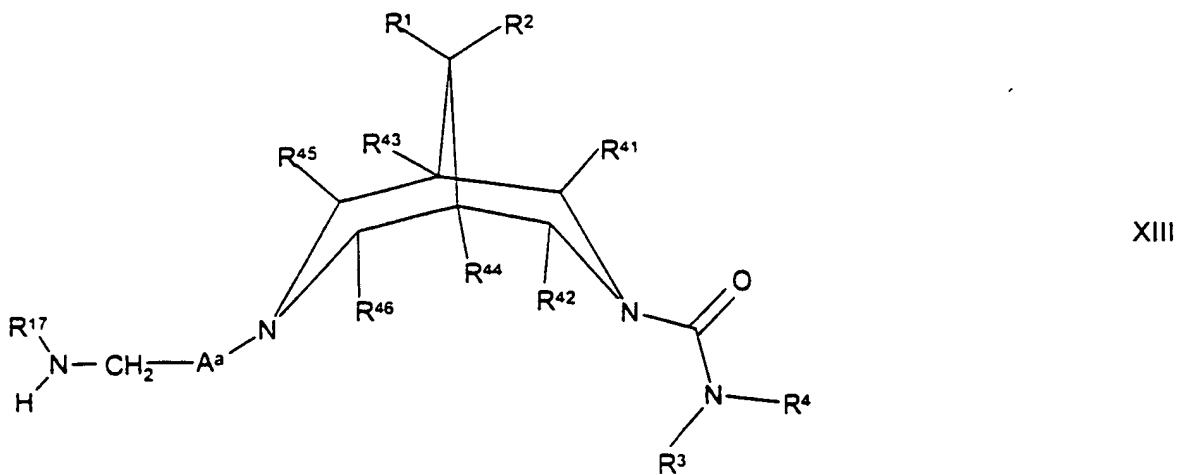
(k) for compounds of formula I which are C₁₋₄ alkyl quaternary ammonium salt derivatives, in which the alkyl group is attached to a bispidine nitrogen, reaction, at the bispidine nitrogen, of a corresponding compound of formula I with a compound of formula XII,

R^bL³

XII

wherein R^b represents C₁₋₄ alkyl and L³ is a leaving group;

(1) for compounds of formula I in which R⁵ and R⁶ represent H, A represents C₁₋₆ alkylene and B represents -N(R¹⁷)(CH₂)_n-, reaction of a compound of formula XIII,



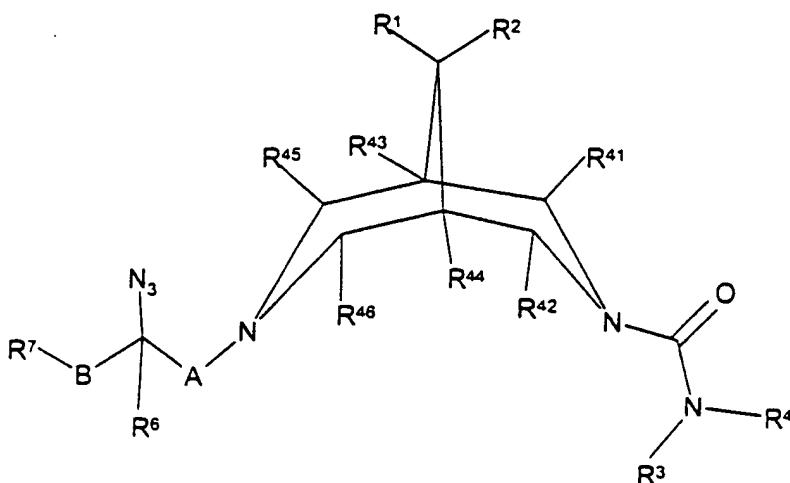
wherein A^a represents C₁₋₆ alkylene and R¹, R², R³, R⁴, R⁴¹, R⁴², R⁴³, R⁴⁴, R⁴⁵, R⁴⁶ and R¹⁷ are as defined in Claim 1 with a compound of formula XIV,



xiv

wherein L^2 is as defined above and R^7 and n are as defined in Claim 1;

(m) for compounds of formula I in which R⁵ represents -NH₂, reduction of a corresponding compound of formula XV,



xv

wherein R^1 , R^2 , R^3 , R^4 , R^6 , R^7 , R^{41} , R^{42} , R^{43} , R^{44} , R^{45} , R^{46} , A and B are as defined

in Claim 1;

(n) for compounds of formula I in which R^5 represents

-N(R¹³)C(O)NH(R¹⁵), reaction of a corresponding compound of formula I in which

R^5 represents $-N(R^{13})H$ with a compound of formula XVI,



XVI

wherein R¹⁵ is as defined in Claim 1;

(o) for compounds of formula I in which R^5 represents $-N(R^{13})C(O)R^{14}$, reaction of a corresponding compound of formula I in which R^5 represents $-N(R^{13})H$ with a compound of formula XVII,



wherein R^X represents a suitable leaving group and R^{14} is as defined in Claim 1;

(p) for compounds of formula I in which R^5 represents $-N(H)R^{12}$, wherein R^{12} is as defined in Claim 1 provided that it does not represent H, reaction of a corresponding compound of formula I, in which R^5 represents $-NH_2$ with a compound of formula XVIII,



wherein R^{12a} represents R^{12} as defined in Claim 1 provided that it does not represent H and L^1 is as defined above;

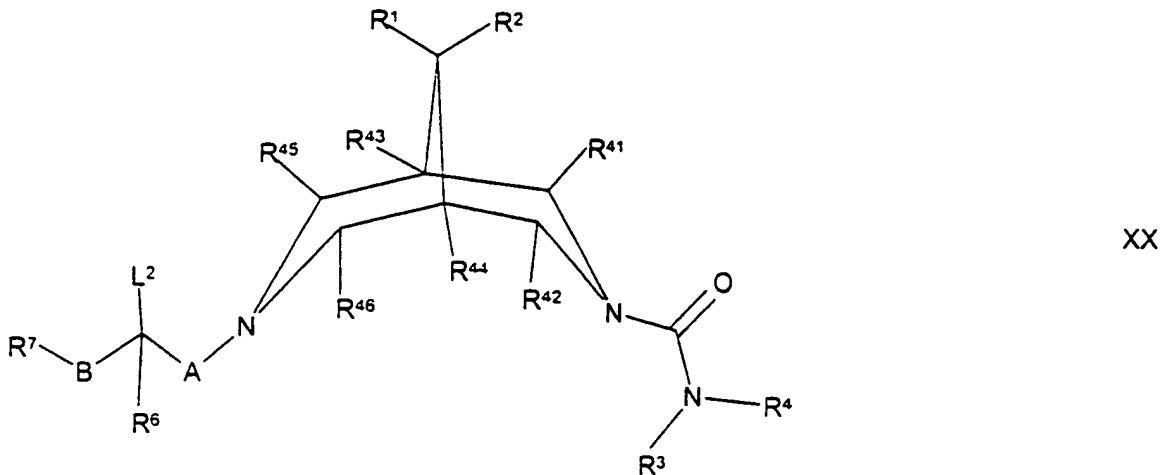
(q) for compounds of formula I in which R^5 represents $-OR^{12}$ in which R^{12} represents C_{1-6} alkyl or optionally substituted aryl, reaction of a corresponding compound of formula I in which R^5 represents $-OH$ with a compound of formula XIX,



wherein R^{12a} represents C_{1-6} alkyl or optionally substituted aryl;

(r) for compounds of formula I in which R^5 represents $-OR^{12}$, in which R^{12}

represents C₁₋₆ alkyl or optionally substituted aryl, reaction of a compound of formula XX,



wherein L² is as defined above and R¹, R², R³, R⁴, R⁶, R⁷, R⁴¹, R⁴², R⁴³, R⁴⁴, R⁴⁵, R⁴⁶, A and B are as defined in Claim 1 with a compound of formula XIX as defined above;

(s) for compounds of formula I in which R⁵ represents OR¹² and R¹² represents C(O)R¹⁴, reaction of a corresponding compound of formula I in which R⁵ represents OH with a compound of formula XXI,



XXI

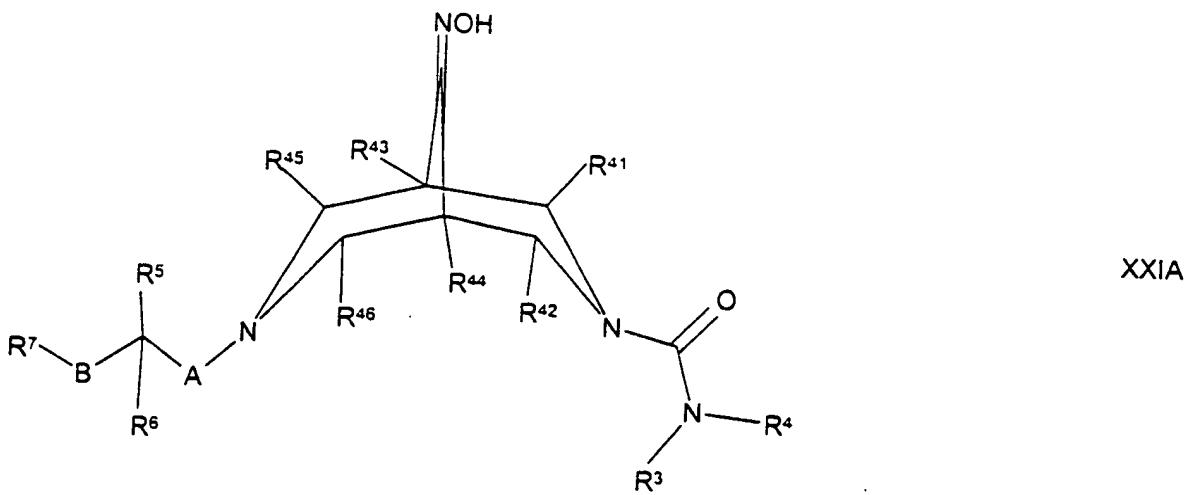
wherein R¹⁴ is as defined in Claim 1;

(t) for compounds of formula I in which R⁵ represents halo, substitution of a corresponding compound of formula I in which R⁵ represents -OH, using an appropriate halogenating agent;

(u) for compounds of formula I in which R³ and/or R⁴ as appropriate represent alkyl groups, alkylation of a corresponding compound of formula I, in which R³ and/or R⁴ (as appropriate) represent H;

(v) conversion of one R^4 group to another;

(w) for compounds of formula I in which one of R^2 and R^3 represents $-\text{NH}_2$ and the other represents H, reduction of a compound of formula XXIA,



wherein $R^3, R^4, R^5, R^6, R^7, R^{41}, R^{42}, R^{43}, R^{44}, R^{45}, R^{46}$, A and B are as defined in

(x) for compounds of formula I in which one or both of R^1 and R^2 represent -
 $N(R^{2c})R^{2d}$ in which one or both of R^{2c} and R^{2d} represents C_{1-6} alkyl, alkylation of a

corresponding compound of formula I in which R¹ and/or R² represent -N(R^{2c})R^{2d} (as appropriate) in which R^{2c} and/or R^{2d} (as appropriate) represent H, using a compound of formula XXIB,

R^{2e}L¹

XXIB

wherein R^{2e} represents C₁₋₆ alkyl and L¹ is as defined above; or

(y) conversion of one substituent on R⁷ to another.

26 (previously presented). A compound of formula II, as defined in Claim 25, provided that R⁷ does not represent optionally substituted phenyl or C₁₋₆ alkyl.

27 (previously presented). A compound of formula V, as defined in Claim 25, provided that R⁷ does not represent optionally substituted phenyl.

28 (previously presented). A compound of formula X as defined in Claim 25.

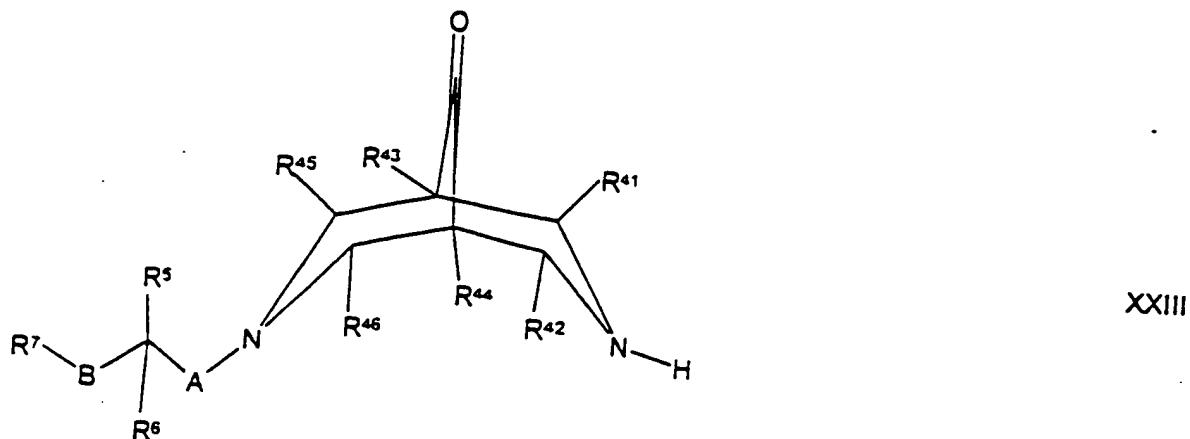
29 (previously presented). A compound of formula XI as defined in Claim 25.

30 (previously presented). A compound of formula XIII, as defined in Claim 25.

31 (previously presented) A compound of formula XV, as defined in Claim 25.

32 (previously presented). A compound of formula XX, as defined in Claim 25.

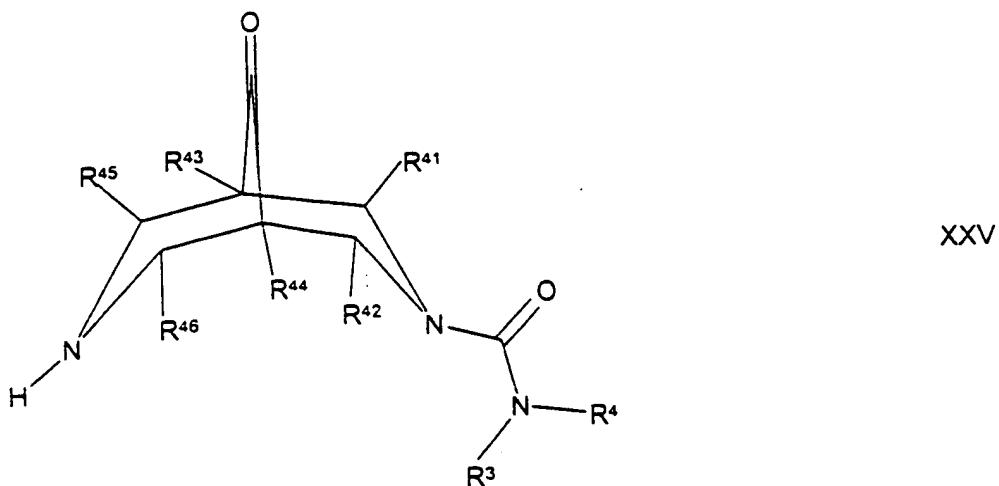
33 (previously presented). A compound of formula XXIII,



XXIII

wherein R⁵, R⁶, R⁴¹, R⁴², R⁴³, R⁴⁴, R⁴⁵, R⁴⁶, A and B are as defined in Claim 1, R⁷ represents aryl or Het², all of which groups are optionally substituted and/or terminated (as appropriate) by one or more substituents selected from -OH, cyano, halo, amino, nitro, Het³, -C(O)R¹⁰, C(O)OR¹¹, C₁₋₆ alkyl, C₁₋₆ alkoxy, -N(H)S(O)₂R¹⁸, -S(O)₂R¹⁹, -OS(O)₂R²⁰, -N(H)C(O)N(H)R²¹, -C(O)N(H)R²² and/or aryl (which latter group is optionally substituted by one or more cyano groups); provided that R⁷ does not represent optionally substituted phenyl, provided that R₇ does not represent C₁₋₆ alkyl or optionally substituted phenyl.

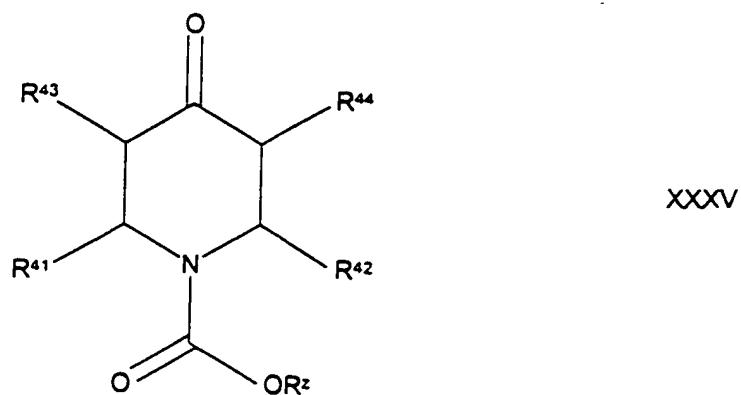
34 (previously presented). A compound of formula XXV,



wherein R³, R⁴, R⁴¹, R⁴², R⁴³, R⁴⁴, R⁴⁵ and R⁴⁶ are as defined in Claim 1.

35 (previously presented). A process for the preparation of a compound of formula X, of formula XXIII, or of formula XXV (in which, in all cases, R⁴⁵ and R⁴⁶ both represent H), which comprises (as appropriate) reaction of either:

- (i) a compound of formula XXXV,



wherein R^z represents C₁₋₁₀ alkyl or C₁₋₃ alkylaryl and R⁴¹, R⁴², R⁴³ and R⁴⁴ are as defined in Claim 1, or

(ii) 4-piperidone with (as appropriate) either:

(1) a compound of formula XXXVI,



wherein R⁵, R⁶, R⁷, A and B are as defined in Claim 1, or

(2) NH₃,

in all cases in the presence of a formaldehyde and, in the case of compounds of formulae X and XXV, followed by conversion of the C(O)OR^z group in the resultant intermediate to a C(O)N(R³)(R⁴) group.

36 (original). A process as claimed in Claim 35, in which the reaction is carried out in the presence of an organic acid.

37 (original). A process as claimed in Claim 36, in which the organic acid is acetic acid.

38 (previously presented). A compound as claimed in Claim 16, wherein the cyano group is in the 4-position relative to B.

39 (previously presented). A method as claimed in Claim 24, wherein the arrhythmia is an atrial or a ventricular arrhythmia.